Remarks

In the Advisory Action, the Examiner first stated that the applicants first argued that the prior art does not teach the genus of pathogens recited in the claims. The applicants respectfully disagree. The applicants first argued that the art does not teach the particular claims of immunogens to achieve the particular results (local and systemic IgA response). The Examiner further stated that Thibodeau teaches "the principal way by which the infectious agents gain access to an organism is through mucosal membranes" as somehow supporting the proposition that Thibodeau teaches administration of the antigens of the claim to the floor of the mouth. But recognition that particular agents gain access through a particular location is not a teaching of a preventive or therapeutic administration at that location. Consider, for example, *Haemophilus influenzae*, which induces meningitides. While this virus gains access to the host organism via the upper respiratory route, the currently commercialized vaccines are all administered parenterally.

With regard to the Examiner's comments on the applicant's second and third points, none of the references, alone or in combination, teach administration to the floor of the mouth in particular. Heiber teaches sublingual administration, which it identifies as including the ventral surface of the tongue and the floor of the mouth, but does not teach administration to the floor of the mouth in particular. Heiber is directed to macromolecular a drug/enhancer/polymer formulation for improving delivery through the buccal and sublingual routes. Nothing in Heiber distinguishes the floor of the mouth from other sublingual locations or the buccal routes. Therefore nothing in Heiber suggests the floor of the mouth in particular.

The Examiner next stated that the art's teaching of administration to the floor of the mouth would inherently result in an immune response in the buccal membranes. This statement has significance only if administration of *any* antigen to the floor of the mouth would induce an immune response in the buccal membranes. This is not the case, however. An antigen is simply a compound that is able to react with an antibody but is not, by definition, a compound able to induce an immune response. An immunogen, by contrast, is a compound able to induce a specific immune response. Heiber *et al.*, for example, teaches a composition a composition comprising heparin for administration via the sublingual and buccal routes. Heparin is an antigen, but clearly Heiber does not wish to induce an immune response to heparin.

Next the Examiner cited Kozlowski *et al.* for the proposition that "a well-documented fact that administration of antigen to one mucosal region may generate S-IgA antibodies at distant mucosal sites." But Kozlowski *et al.* is directed to comparing mucosal immunization with cholera vaccine of the rectum and female genital tract by immunizing orally, rectally, or vaginally to induce an immune response in the rectal and genital tract secretions. This is very different from the presently claimed invention.

Moreover, after making the above-quoted stated regarding generation of S-IgA antibodies at distant mucosal sites, Kozlowski *et al.* goes on to state, "On the other hand, there is evidence that local exposure to antigen can result in much higher levels of specific IgA in the region of exposure than at distant sites." p. 1387, col. 2. In addition, in the abstract Kozlowski *et al.* states, "In addition, local production of CTB-specific IgG in the genital tract could be demonstrated only in vaginally immunized women. Vaginal immunization did not generate antibodies in the rectum, however." Thus, at best Kozlowski *et al.* contains mixed teachings and does not provide the ordinary artisan with a reasonable expectation that administration to the floor of the mouth would result in an immune response in the buccal membrane, as the Examiner suggested.

The Examiner next dismissed the applicants' argument regarding the inapplicability of the results in rabbits to primates, asserting that the applicants' statement in the specification to this effect is insufficient. The applicants respectfully submit, however, that burden is on the Examiner to establish a *prima facie* case of obviousness, and part of this burden is presenting evidence that the results in rabbits are indicative of the results one would achieve in primates. This has yet to be done.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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